

A case of sebaceous adenoma of the eyelid showing excessively rapid growth

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Background: Sebaceous adenomas are found mainly in elderly individuals and are usually tan, pink, or yellow nodules or papules, usually approximately 5 mm in the largest size.

Case report: A 65-year-old man presented with a progressively enlarging exophytic lesion in the right eyelid for 3 months. External examination revealed a yellowish-pink growth measuring 18 × 13 × 14 mm. The lesion surface was covered by palpebral conjunctiva with fine papillary projections, vascularity, crusting, and ulceration. Two weeks later, the growth enlarged to 20 × 14 × 14 mm, and ulceration also expanded. An excisional biopsy with clear resection margins was performed. No malignancy was found in the stump. Histopathologically, the lesion was located principally within the cutaneous compartment and composed of multiple circumscribed sebaceous lobules, separated, and exhibiting no cytologic atypia. Cystic change was not evident, and no infiltrative growth pattern, pagetoid lesions, mitotic figures, and lymphovascular space invasion were observed. The Ki-67 nuclear antigen was detected in 10%–15% of cells located in the basal zone of the nodule. Fluorescence in situ hybridization showed low human epidermal growth factor receptor 2 amplification, suggesting no genetic changes. The clinical findings, lack of infiltrative border, low Ki-67 index, and low proliferative ability support a diagnosis of sebaceous adenoma.

Conclusion: Sebaceous adenoma that shows excessively rapid growth due to hyperplasia may appear to be malignant. Histopathology, fluorescence in situ hybridization, and Ki-67 were useful to the diagnosis of the adenoma. Excisional biopsy with clear resection margins must be performed in rapidly growing tumors.

Keywords: sebaceous adenoma, Ki-67, fluorescence in situ hybridization, sebaceous carcinoma

Introduction

Sebaceous lesions of the eyelid may involve the glands of Zeiss or meibomian glands. Sebaceous hyperplasia, or senile sebaceous nevus, and sebaceous adenomas occur mainly on the face and scalp of individuals aged 60 years, on average.^{1,2} Sebaceous adenomas were first reported by Van Walbeek³ in 1949, and were characterized as benign tumors that present clinically as tan, pink, or yellow nodules or papules, usually approximately 5 mm in the largest size.^{2,4} Like most sebaceous proliferations, these tumors typically arise in the head and neck regions of older individuals,¹ although sebaceous neoplasms in the eyelid associated with Muir–Torre syndrome have been reported.^{5–7} Most sebaceous carcinomas arising in the periocular region of elderly patients are aggressive lesions. Extraocular forms are rare, small, and appear to be less aggressive. We report a case of a rapidly growing form – one of the largest sebaceous adenomas of the eyelid.

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Case report

A 65-year-old man was referred to our hospital and presented with an exophytic lesion involving the right lower eyelid, which had enlarged progressively for the last 3 months. There were no family and medical histories of ocular disease or any malignancy. At first presentation, the patient's corrected visual acuity was 20/20 oculi uterque, and intraocular pressure of the right eye was 18 mmHg. No remarkable changes were found in the anterior chamber, lens, vitreous, and fundus of both eyes. The mobility and position of the right eyeball were within normal limits.

External examination revealed a yellowish-pink, warty growth at the right lower eyelid, close to the margin, measuring $18 \times 13 \times 14$ mm. The surface of the lesion was covered by the palpebral conjunctiva and showed fine papillary projections, vascularity, crusting, and ulceration. There were no surrounding induration, madarosis, pain, and discharge (Figure 1A). Muir–Torre syndrome was considered; therefore, a systemic examination was performed, and no malignant suspected lesion was found. A test for the human immunodeficiency virus, linked to sebaceous adenoma,⁵ was negative.

After 2 weeks, the lesion had grown rapidly. The mass enlarged to $20 \times 14 \times 14$ mm. The crusting, vascularity, and ulceration in the center of the lesion surface also expanded (Figure 1B). A malignant tumor, possibly a sebaceous carcinoma, was suspected. An excisional biopsy with clear resection margins was performed. Macroscopically, the eyelid lesion was composed of a pentagonal piece of skin measuring $20 \times 14 \times 14$ mm, with a firm yellow exophytic nodule. Microscopic examination demonstrated an exophytic neoplasm, located mainly within the cutaneous compartment. It was composed of multiple irregularly shaped, closely packed, circumscribed sebaceous lobules, separated by compressed dermal connective tissue septa.

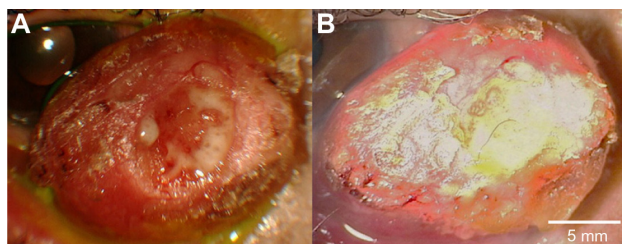


Figure 1 Clinical findings at presentation and 2 weeks later. Clinical findings at presentation (A) and 2 weeks later (B). (A) At presentation, a yellowish-pink, warty mass in the right lower eyelid, close to the margin, measuring $18 \times 13 \times 14$ mm was observed. The lesion surface had fine papillary projections with vascularity, crusting, and ulceration. (B) Two weeks later, the mass had enlarged to $20 \times 14 \times 14$ mm.

Note: Vascularity and ulceration also expanded.

The lobules communicated with the epidermal surface via several openings. Each lobule was composed of a peripheral mitotically active basaloid germinative layer, exhibiting no cytologic atypia and maturing to vacuolated sebocytes in the center. Transitional cell forms were seen (Figure 2A). The lesional tissue is composed of mostly mature central sebocytes. Variable eosinophilic holocrine degeneration was not seen. Meibomian architecture changes were not found. No definitive cystic change was identified, nor were infiltrative growth patterns or pagetoid lesions. Intrinsic vascularity was of normal formation, and lymphovascular space invasion was evident. The eyelid tissue adjacent to the lesion exhibited patchy focal lipogranulomatous inflammation, indicating secondary chalazion formation. There was no malignancy in the stump.

Immunohistochemical study detected Ki-67 in 10%–15% of the sebaceous nodular cells localized in the basal zone of the nodules (Figure 2B). The Ki-67 index was lower than in normal cutaneous tissues (6.8%) without a nodular lesion.⁶ Fluorescence in situ hybridization (FISH), which detects genetic changes in human epidermal growth factor receptor 2 (HER2) that give rise to human tumors, was performed. However, the cells showed low HER2 gene amplification and no increase in metaphase cells, indicating no genetic changes. The findings of a circumscribed lesion, mature sebaceous phenotype, lack of infiltrative borders, absence of aberrant mitotic figures, low Ki-67 index, and low proliferative ability support a diagnosis of sebaceous adenoma. The patient was followed up after 2 years 6 months; any regrowth was not found.

This case report did not require Institutional Review Board/Ethics Committee approval.

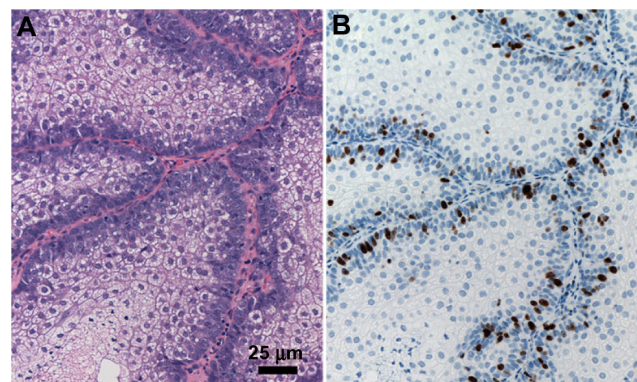


Figure 2 Hematoxylin and eosin staining and Ki-67 immunohistochemical staining of the excised mass. (A) Hematoxylin and eosin staining and (B) Ki-67 immunohistochemical staining of the excised mass. Original magnification $\times 100$. (A) The lobules communicate with the epidermal surface via several openings. Each lobule is composed of a peripheral, mitotically active, basaloid germinative layer, exhibiting no cytologic atypia and maturing to vacuolated sebocytes in the center. Transitional forms are seen. (B) Ki-67 nuclear antigen is positive in 10%–15% of the sebaceous nodular cells located in the basal zone of nodule.

Discussion

The general features of sebaceous adenomas have been reported as follows: approximately 5 mm in greatest dimension,² maintaining a lobular and organoid architecture, and often showing connection with or replacement of the overlying squamous epithelium.⁷ Expansion and increased prominence of the peripherally located basaloid cells are key discriminators between sebaceous hyperplasia and sebaceous adenoma or sebaceoma. Sebaceous adenomas show variably expanded basaloid cells, more than the normal two-cell layers seen in normal sebaceous glands and sebaceous hyperplasia, but by convention < 50% of the tumor cell volume (>50% basaloid cell content is seen in sebaceoma).

In the present case, the yellowish-pink nodule measured 20 × 14 × 14 mm, which exceeded the reported size for sebaceous adenomas. The growth speed estimated from clinical findings was 1.19 times in 14 days, thus the tumor volume doubling time was estimated to be 57 days, reflecting more rapid growth than found in usual neoplasms.

Macroscopically, the surface of the mass exhibited vascularity, crusting, and ulceration, and these lesions enlarged and deepened 2 weeks later, suggesting malignant changes. However, microscopically, the mass maintained a lobular and organoid architecture and had connections with the overlying squamous epithelium. The nodule showed variably expanded basaloid cells, with more than the normal two cell layers seen in normal sebaceous glands, but no tumor cell was detected. Ki-67 nuclear antigen is expressed in G1, S, G2, and M phases of the cell cycle, but it is undetectable in G0.⁸ Recently, antibodies to formalin-resistant epitopes of the Ki-67 protein are regarded as the most reliable indicators of cellular proliferation.⁶ The Ki-67 index of sebaceous carcinoma was reported to range from 26%–50%.⁸ In the present case, the Ki-67 index was 10%–15%, indicating a low proliferative speed and excluding malignant dysplasia. Past reports suggested an inverse correlation between the log tumor volume doubling time and Ki-67 index.⁹ In the present case, the rapid growth indicated malignancy, but the Ki-67 index suggested otherwise.

The lesion in the present case grew excessively rapidly. The sebaceous adenoma was derived from the sebaceous gland in the inner zone of the eyelid. We suspect that when the adenoma growing in the inner eyelid broke the bulbar conjunctiva, the growth that had reached a substantial size underneath was pushed out from the break, resulting in the apparent rapid increase in tumor size over a short period of time. Thus, the lesion was diagnosed as sebaceous adenoma, which is conventionally a slow-growing tumor with exophytic extension.

In the present study, the excision of the tumor was complete, and an excisional biopsy found sebaceous adenoma. The utility of excisional biopsy for diagnosis was past reported.^{10–12} When the excision was subtotal, the tumor may rapidly regrow and transform into malignancy.¹³ When malignancy was suspected, excisional biopsy with clear resection margins must be performed in rapidly growing tumors.

In general, an excessively rapid growing lesion is highly suspicious of being malignant. As this case demonstrated, a sebaceous adenoma may appear to grow rapidly under special circumstances. Histopathology, FISH, and Ki-67 were useful in diagnosing the adenoma. Excisional biopsy with clear resection margins must be performed in rapidly growing tumors.

Disclosure

The authors report no conflicts of interest in this work. None of the authors had financial or personal conflict of interests with regards to this study.

References

1. Iwasaki J, Yoshida Y, Yamamoto O, Tajima S. Poroma with sebaceous differentiation of the eyelid: a rare site of occurrence. *Acta Derm Venereol.* 2008;88(2):166–167.
2. Deprez M, Uffer S. Clinicopathological features of eyelid skin tumors. A retrospective study of 5504 cases and review of literature. *Am J Dermatopathol.* 2009;31(3):256–262.
3. Van Walbeek K. Adenoma of a sebaceous gland of the lacrimal caruncle. *Ophthalmologica.* 1949;117(6):370.
4. Maino JH, Richer SP, McGregor D. Caruncle lesions: the use of histological evaluation in determining a definitive diagnosis. *J Am Optom Assoc.* 1983;54(6):521–524.
5. Short KA, Williams A, Creamer D, Fuller LC. Sebaceous gland hyperplasia, human immunodeficiency virus and highly active anti-retroviral therapy. *Clin Exp Dermatol.* 2008;33(3):354–355.
6. Ohara M, Sotozono C, Tsuchihashi Y, Kinoshita S. Ki-67 labeling index as a marker of malignancy in ocular surface neoplasms. *Jpn J Ophthalmol.* 2004;48(6):524–529.
7. Moscarella E, Argenziano G, Longo C, et al. Clinical, dermoscopic and reflectance confocal microscopy features of sebaceous neoplasms in Muir-Torre syndrome. *J Eur Acad Dermatol Venereol.* Epub April 4, 2012.
8. Auw-Haedrich C, Sundmacher R, Freudenberg N, et al. Expression of p63 in conjunctival intraepithelial neoplasia and squamous cell carcinoma. *Graefes Arch Clin Exp Ophthalmol.* 2006;244(1):96–103.
9. Tanaka Y, Hongo K, Tada T, Sakai K, Kakizawa Y, Kobayashi S. Growth pattern and rate in residual nonfunctioning pituitary adenomas: correlations among tumor volume doubling time, patient age, and MIB-1 index. *J Neurosurg.* 2003;98(2):359–365.
10. Sivagurunathan A, Goodhead AD, Du Plessis EC. Multiple eyelid apocrine hidrocystoma in a domestic short-haired cat. *J S Afr Vet Assoc.* 2010;81(1):65–68.
11. Park DY, Lee JH, Suh YL, Woo KI, Kim YD. Metastatic adenoid cystic carcinoma of the eyelid. *Ophthalm Plast Reconstr Surg.* 2012;28(5):e111–e112.
12. Dailey RA, Chavez MR. Upper eyelid margin mass excision technique: supraciliary approach. *Ophthalm Plast Reconstr Surg.* 2011;27(1):48–51.
13. Jakobiec FA, Zimmerman LE, La Piana F, Hornblass A, Breffell RA, Lackey JK. Unusual eyelid tumors with sebaceous differentiation in the Muir-Torre syndrome. Rapid clinical regrowth and frank squamous transformation after biopsy. *Ophthalmology.* 1988;95(11):1543–1548.

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